

is derived is JEV. In some embodiments of the invention, the *Flavivirus* from which the capsid protein is derived is SLEV. In some embodiments of the invention, the *Flavivirus* from which the capsid protein is derived is YFV. In some embodiments of the invention, the *Flavivirus* from which the capsid protein is derived is DENV. In some embodiments of the invention, the

5 *Flavivirus* from which the capsid protein is derived is WNV.

The invention provides, *inter alia*, methods of inducing the death of cells using capsid proteins and other proteins from viruses including *Flavivirus* or *Pestivirus*, or functional fragments thereof. In some embodiments the capsid protein, or functional fragments thereof are from WNV. The invention also provides methods of screening for compounds that inhibit the cell killing activity of capsid protein and other proteins from viruses including *Flavivirus* or *Pestivirus*, or functional fragments thereof. In some embodiments of the invention, methods are provided for screening for compounds that inhibit the cell killing activity of WNV capsid protein, or functional fragments thereof. The invention further provides pharmaceutical compositions comprising capsid proteins or other proteins from viruses including *Flaviviruses* or *Pestiviruses*, or functional fragments thereof, or nucleic acids encoding capsid proteins or other proteins from viruses including *Flaviviruses* or *Pestiviruses*, or functional fragments thereof, and methods of treating individuals having diseases characterized by hyperproliferating cells with these pharmaceutical compositions. The invention further provides vaccine compositions comprising capsid proteins or other proteins, or fragments thereof, or nucleic acids encoding capsid proteins or other proteins, or functional fragments thereof, from WNV or from other viruses including *Flaviviruses* or *Pestiviruses* and a pharmaceutically acceptable carrier. The invention also provides diagnostic methods and kits for identifying individuals exposed to WNV or other viruses including *Flaviviruses* or *Pestiviruses*.

25 The practice of the present invention employs, unless otherwise indicated, conventional methods of virology, immunology, microbiology, molecular biology and recombinant DNA techniques within the skill of the art. Such techniques are explained fully in the literature. See, e.g., Sambrook *et al.*, eds., *Molecular Cloning: A Laboratory Manual* (2<sup>nd</sup> ed.) Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY (1989); Ausubel *et al.*, eds., *Current Protocols in Molecular Biology*, John Wiley & Sons, New York, NY (2000); Glover, ed., *DNA Cloning: A Practical Approach*, Vols. I & II; Colowick & Kaplan, eds., *Methods in Enzymology*, Academic Press; Weir & Blackwell, eds., *Handbook of Experimental Immunology*, Vols. I-IV, Blackwell Scientific Pubs. (1986); Fields, Knipe, & Howley, eds., *Fields Virology* (3<sup>rd</sup> ed.) Vols.

I & II, Lippincott Williams & Wilkins Pubs. (1996); Coligan *et al.*, eds., Current Protocols in Immunology, John Wiley & Sons, New York, NY (2000), each of which is incorporated herein by reference.

Various definitions are made throughout this document. Most words have the meaning that would be attributed to those words by one skilled in the art. Words specifically defined either below or elsewhere in this document have the meaning provided in the context of the present invention as a whole and as typically understood by those skilled in the art.

As used herein, the terms “induce” and “inducing” in reference to cell death or apoptosis refer to activities that initiate events that lead to cell death, including activities that initiate cellular events that are part of an apoptotic pathway that contribute to cell death.

As used herein, the term “apoptosis” refers to the form of eukaryotic cellular death, which is distinct from necrosis, and which includes cytoskeletal disruption, cytoplasmic shrinkage and condensation, expression of phosphatidylserine on the outer surface of the cell membrane and blebbing, resulting in the formation of cell membrane bound vesicles or apoptotic bodies. For a review of apoptotic cell death see, *e.g.*, Utz & Anderson, 2000, Life and death decisions: regulation of apoptosis by proteolysis of signaling molecules, Cell Death Differ., 7:589-602, which is incorporated herein by reference.

As used in this specification and the appended claims, the singular forms “a,” “an” and “the” include plural references unless the content clearly dictates otherwise. Thus, for example, reference to “a cell” includes a mixture of two or more cells.

As used herein, the phrases “amount effective to induce cell death” and “level effective to induce cell death” in reference to capsid protein, or functional fragments thereof, means that the amount of capsid protein, or functional fragment thereof, in contact with a cell, or the level of capsid protein, or functional fragment thereof, expressed in the cell, is effective to trigger the events that will kill the cell.

As used herein, the term “protein” refers to a polymer of amino acid residues, and is not limited to a minimum length. Polypeptides, peptides, oligopeptides, dimers, multimers, and the like, are included in the definition. Both full length proteins and fragments thereof are contemplated by the definition. The term also includes post-expression modifications to the protein, including, but not limited to, glycosylation, acetylation, phosphorylation.

As used herein, the phrase “functional fragment thereof” in reference to capsid protein, refers to fragments of less than the full length of the protein that maintain the function of the capsid protein, and are capable of inducing cell death or inducing apoptosis.

As used herein, the phrase “immunogenic fragment thereof” in reference to capsid protein, refers to fragments of less than the full length of the protein against which an immune response can be induced.

As used herein, “nucleic acid” includes DNA and RNA, as well as modified forms thereof, including modified sugars, bases, or backbone.

As used herein, the phrase “free from an entire *Flavivirus* or *Pestivirus* genome” used in reference to a nucleic acid encoding a capsid protein, or functional fragment thereof, indicates that the nucleic acid is in a form that is in a recombinant form or construct, or that it is otherwise isolated from its natural state in a *Flavivirus* or *Pestivirus* genome.

As used herein, the phrase “free from an entire WNV genome” used in reference to a nucleic acid encoding a capsid protein, or functional fragment thereof, indicates that the nucleic acid is in a form that is in a recombinant form or construct, or that it is otherwise isolated from its natural state in a WNV genome.

As used herein, “detectable level” in reference to apoptosis, means that the level or amount of apoptosis elicited is at a threshold level that can be detected or measured by techniques known to those of skill in the art. Detection techniques depend on the identification of the presence or increased presence of “markers of apoptosis.”

As used herein, “marker of apoptosis” refers to cellular factors or morphological changes that serve as indicators that apoptosis has been triggered and that cells are undergoing apoptotic death. “Markers of apoptosis” include, but are not limited to, exposed cellular membrane phosphatidylserine (PS), free 3'-hydroxy DNA termini, and cytoplasmic nucleosomes.

As used herein, the term “compound” in reference to inhibitors of WNV or other viruses including *Flaviviruses* or *Pestiviruses* capsid or other protein apoptosis-inducing activity includes, but is not limited to, any identifiable chemical or molecule, including, but not limited to small molecules, peptides, polypeptides, proteins, sugars, nucleotides, or nucleic acids. Such compounds can be natural or synthetic.

As used herein, “inhibit” in reference to WNV or other viruses including *Flaviviruses* or *Pestiviruses* capsid or other protein apoptosis-inducing activity, refers to any interference with this activity. For example, the term “inhibit” includes both the elimination and reduction of